UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,851	06/05/2000	HANS ACHENBACH	A32964PCT/U	6879

21003 7590 01/16/2004

BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
PATTEN, PATRICIA A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/463,851	ACHENBACH, HANS	
	Examiner	Art Unit	
	Patricia A Patten	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53,57,59,60 and 63-80* is/are pending in the application.

4a) Of the above claim(s) *74-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53,57,59,60 and 63-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

RCE Practice

A request for continued examination under 37 CFR § 1.114, including the fee set forth in 37 CFR § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR § 1.114, and the fee set forth in 37 CFR § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR § 1.114. Applicant's submission filed on 12/04/2003 has been entered.

Claims 53, 57, 59-60, 63-71 and 72-80 are pending in the application.

Claims 74-80 were withdrawn from further consideration on the merits for being directed toward a non-elected invention in the Office Action dated 5/30/2003.

Claims 53, 57, 59-60, 63-71 and 72-73 were examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53, 57, 59-60, 63-64 and 72-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting plant fungal growth *in-vitro* or inhibiting mutagenesis caused by 2-nitrofluorine or 2-aminoanthracene in a microorganism via administration of an organic solvent extract of *Aristolochia taliscana*, does not reasonably provide enablement for a method for inhibiting all mutagenesis by all known mutagens in all organisms or inhibiting fungal growth in any organism such as mammals.

Applicants arguments were fully considered, but not found persuasive for the following reasons:

Applicants argue that the claims are not broad enough to cover mutagenesis which may cover cancer. Applicant argues that the claims are limited therefore to nucleic acid mutations. The Examiner maintains that the Instant claims are broad enough to cover cancerous cells, because it is the Examiner's opinion that a 'mutation' is not limited to only a DNA mutation, but phenotypical consequences thereof. However, considering *arguendo* that the claims are drawn more narrowly to nucleic acid mutations, the Instant claims are still not in compliance with the scope of enablement as required by the statute of 35 USC 112 First paragraph because the skilled artisan could not make any reasonable correlation between the inhibition of two specific mutagens to

a specific strain of bacteria and ***inhibition of all known mutagens to all known organisms.***

Applicants argue that "...the ability of Aristolochia taliscana extracts to inhibit the mutagenesis of any given compound can be easily tested using the Ames test, followed by routine animal testing to verify *in vivo* activity" (p.6-Arguments). Thus, Applicants are contending that that 35 U.S.C. § 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. However, the issue here is the breadth of the claims in ***light of the predictability of the art*** as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This 'make and test' position is inconsistent with the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 13 USPQ2d, 1737 (1990), and *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

With regard to the propriety of specifically considering the decisions of *In re Fisher*, *Amgen Inc. v. Chugai*, and *In re Wands* to the exclusion of the plurality of decisions cited by Applicant in determining the patentability of the instant claims, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph in a

recent CAFC decision, *Genentech, Inc. v. Novo Nordisk*, 42 USPQ2d, 100 (CAFC 1997), in which these three decisions were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. *To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound.* Unless one has a **reasonable expectation** that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are **more likely to work that not** without actually making and testing them then the instant application does not support the breadth of the claims.

In the Instant case, Applicants have demonstrated the efficacy of an *A.taliscania* extract on inhibition of two known mutagens, 2-amino-anthracene (2AA) and 2-nitrofluorene (2NF). The Examiner previously set forth the unpredictability concerning the *in-vivo* enablement for these methods (please see previous Office Action). Applicants argue that "If it is the Examiner's contention that the Ames test is not accepted as a means of establishing mutagenicity and predicting in vivo mutagenic

activity, then, Applicant respectfully request[s] support for that contention" (p.6-Arguments). While it is accepted that the Ames test is a good test for establishing mutagenicity, and further establishing inhibition of mutagenic agents, it is not accepted that the Ames test is directly correlated to clinical outcome (*in-vivo*). The efficacy of a drug treatment *in-vivo* faces unfavorable obstacles not present in *in-vitro* models. As such, in vivo utility necessarily involves unpredictability with respect to physiological activity of an asserted process in humans as well as animal models. See discussion in Ex parte Kranz, 19 USPQ 2d 1216, 1218-1219 (6/90). For examples, drug delivery to the target area must survive the acidic environment of the stomach if administered orally. Additionally, the delivery of the drug across necessary cell surfaces in amounts needed to be efficacious, but not lethal to the subject, necessitates sensitive testing in order to adequately determine the proper human dosage. The specification does not provide such guidance and fails to provide any correlation between inhibition of 2NF and 2AA *in-vitro* in bacterial cells to inhibition in any other cell such as mammalian or avian for example, routes of delivery (e.g. intratumoral, intravenous etc.) or dosage amounts/frequencies. Without such guidance in the specification and the lack of correlative working examples, the claims would ***require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.***

In the instant case, it is highly improbable that an extract of *A.taliscania* will prevent *all mutations* caused by *all mutagens* in *all organisms* due to the plethora of

known mutagens, plants, animals and microorganisms and the vast differences with regard to their individual biochemical mechanisms. The skilled artisan could not make any *reasonable extrapolation* between inhibition of Salmonella by 2AA and 2NF to all microorganisms especially because no mechanism of action has been established in order to perform a reasonable correlation. It is not known if the *A.taliscana* extract inhibited the compounds *per se*, or alternatively, modified some other aspect of the bacteria which rendered the bacteria unresponsive to the mutagens (i.e., change in the bacterial cell wall) or was simply toxic to the microorganisms, making genetic revertants impossible (i.e., no cultures seen on the culture disks). In this respect, the Examiner reasonably concludes that 2AA and 2NF may be inhibited *via some unknown mechanism, but* it is not absolutely clear that the inhibition is due to compound-compound (or alternatively extract-compound) interactions.

It remains deemed therefore, that the amount of experimentation would proceed far beyond the level of reason in order to actually carry out the claimed invention due to the enormous breadth of the claims. The skilled artisan would necessarily be required to test *every known mutagen* on *every known species of organism* to ascertain the effectiveness of the claimed method. This experimentation would be undue considering the ***great lengths of time and expense*** that would incur upon such experimentation. The inadequate disclosure coupled with a lack of representative examples and the art recognized unpredictability thus preclude the use of *Aristolochia taliscana* extracts

within the scope of the presently claimed invention by the skilled artisan without undue experimentation.

Applicants argue again that "...although the specification only disclosed the use of plant fungus species, it would be routine to substitute fungal species that infect mammals such as *Candida albicans*, *Aspergillis fumigatus*, *Trichophyton mentagrophytes* and *Cryptococcus neoformans*, and that such substitutions would not require undue experimentation". It remains the opinion of the Examiner that the disclosure does not support the breadth of the claimed invention with regard to fungus which infect mammals due to the lack of guidance within the Instant specification. All of these cited fungi are different genus/species and all possess unique physiological characteristics. The plant fungal species which were shown in the Instant specification to be inhibited by *A. taliscana* do not represent all other fungal species known in the art. The skilled artisan would not expect that an agent which inhibits one fungal species to inhibit any other because the nature of fungal virility is unpredictable in nature. *Candida albicans* is especially difficult to inhibit *in-vivo* as is well known in the art and evidenced by Di Cecco (US 2002/0129443) [0079].

With respect to the adequacy of disclosure that a claimed genus possesses an asserted utility, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if it would be deemed likely by one skilled in the art, in view of contemporary knowledge in the art, that the claimed genus would

possess the asserted utility. In re Oppenauer, 31 CCPA 1248, 143 F.2d 974, 62 USPQ 297; In re Cavallito et al., 48 CCPA 711, 282F.2d 357, 127 USPQ 202. ***For both adequate disclosure and/or enablement requires representative examples which provide reasonable assurance to one skilled in the art that the extract falling within the scope of a claim possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention***. See In re Riat et al. CCPA 1964 327 F2d 685, 140 USPQ 471; In re Barr et al. CCPA 1971 444 F2d 349, 151 USPQ 724, for enablement and for disclosure see Court of Appeals for the Federal Circuit decision, The Regents of the University of California v. Eli Lilly and Company which can be found at the Federal Circuit web site, www.fedcir.gov as file 96-1175.

In the Instant case, the skilled artisan would not have any reasonable assurance that the A.taliscania extract would perform beneficially on any type of fungus besides the specific plant fungi that were demonstrated in the Instant specification. The worker of ordinary skill in the art would not be able to practice the invention as claimed, given the limited and incomplete description set forth in the Specification. Nowhere in the Specification, as filed, is there a full, clear, concise, and exact description of a method for inhibiting any fungi besides the ones Instantly demonstrated.

Claims 65-70 and 72-73 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an extract from *A. taliscana* prepared via benzene extraction to produce a product containing 'at least 10% by weight of a eupomatenoid', does not reasonably provide enablement for any organic solvent extract which will provide for this product. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It has been recognized that Applicants are not entitled to the scope of these claims because there is no indication within the Instant specification that *any* organic solvent extract such as alcohol, will provide for an extract which contains 'at least 10% by weight of a eupomatenoid'. Applicants argued that de la Parra did not teach the specifics of the compound, and thus, do not anticipate the claimed compound. The Examiner concedes. However, it is deemed that because the claims are in product-by –process form, that the type of organic solvent which is used to produce this particular product is a crucial element to the claimed invention. Although Applicants have demonstrated that a benzene extract will successfully extract 'at least 10% by weight [of the extract] of a eupomatenoid', the skilled artisan would not expect that any organic solvent would produce similar results because of the wide range of polarities of organic solvents as well as the solubility factors of eupomatenoids. Chloroform for example, would not be expected to extract the same phytochemical constituents as benzene; nor would hexane, methanol, ethanol, acetonitrile, toluene, DMF, TMF, N-

would hexane, methanol, ethanol, acetonitrile, toluene, DMF, TMF, N-methylpyrrolidone, tetrahydrofuran, methylene chloride, toluene, xylene, n-hexane, cyclohexane, n-heptane, acetone, ether, acetic acid, kerosine or mixtures thereof. Considering the numerous organic solvents known in the art, the skilled artisan would need to perform undue experimentation, involving rigorous trial and error protocols in order to ascertain what other organic solvents will produce the claimed invention. The skilled artisan would perform this experimentation without any reasonable expectation of success because the skilled artisan would reasonably ascertain that each respective organic solvent would extract different percentages of each phytochemical due to their respective polarities/solubilities of the phytochemical constituents in the respective solvents.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A Patten whose telephone number is (703) 308-1189. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-3906.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Patricia A Patten
Examiner
Art Unit 1654

12/19/03

PATRICIA PATTEN
PATENT EXAMINER